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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,310	01/11/2002	Rajendra Singh	SURR.85	6784

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EXAMINER

GAKH, YELENA G

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 08/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/044,310

Applicant(s)

SINGH ET AL.

Examiner

Yelena G. Gakh, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 11-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 11-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment and Remarks filed on 05/10/04 are acknowledged. Claims 1-6 and 11-30 are pending in the application.

Response to Amendment

2. The grounds for rejection of the pending claims are changed in view of the Applicant's arguments and the amendment.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method comprising MS⁴ tandem mass spectrometry, does not reasonably provide enablement for any other mass spectrometry. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification explicitly discloses, "the MS² spectra and MS³ spectra were essentially identical for the two species [PGD₂ and PGE₂] at all ionization energies" (page 6, lines 31-32), which makes it impossible for any routineer in the art to distinguish MS² and MS³ spectra of PGD₂ and PGE₂ at any energy and therefore to perform the method recited in claims 2 and 19.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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6. Claims 11 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The specification discloses only two isomers, PGD₂ and PGE₂ as isobaric isomers. No other isobaric isomers of prostaglandins are disclosed in the specification. Therefore, it is not clear if there are any other prostaglandin isomers, which are isobaric, or this is the only pair of isobaric prostaglandins. This uncertainty renders the claims indefinite.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. **Claims 1, 3-5, 11-18 and 20-30** are rejected under 35 U.S.C. 103(a) as being unpatentable over or Li (PNAS, 1999, IDS) in view of Kamel (Anal. Chem., 1999) and Technical Note (CE-ESI-MS: An Integrated Solutions, on-line 2000).

Li teaches "quantitative high performance liquid chromatography/tandem mass spectrometric analysis of the four classes of F₂-isoprostanes [free radical catalyzed prostaglandin isomers] in human urine"; the sheath flow comprises CH₃O:D₂O. HPLC is performed under acidic conditions with the mobile phase consisted of acetonitrile: methanol with 0.0005% acetic acid adjusted to pH 5.7 with ammonium hydroxide. ESI-MS analysis is performed in the negative ion mode.

Li does not specifically disclose using adding basic liquid to create a sheath flow.

Kamel indicates, "in the negative ion mode, 50 mM ammonium hydroxide gave the greatest sensitivity for [M-H]⁻ ions" (Abstract). Moreover, the Technical Note indicates: "typically the sheath liquids is composed of 10-100% organic solution (methanol, ethanol, iso-propanol, acetonitrile) with acidic (0.1-1.0% acetic or formic acid or ammonium salts, 5-50 mM) or basic (0.1-1.0% ammonium hydroxide) modifier, depending on the required ionization. Optimization of the sheath liquid composition is part of method development, which is facilitated with the fully automated system described here" (Sheath Liquid).

It would have been obvious for anyone of ordinary skill in the art to slightly modify Li's method by adding NH₄OH solution directly to the HPLC eluent comprising prostaglandins, because Kamel demonstrates that presence of NH₄OH leads to the greatest sensitivity for [M-H]⁻ ions in negative mode and NH₄OH is already present in Li's eluent, while in insufficient amount; also the Technical Note indicates that optimization of the sheath liquid composition is part of method development and can be easily done in the automated mode. Therefore, the method comprising adding additional ammonium hydroxide to Li's eluent has reasonable expectation of success for performing separation of prostaglandin isomers disclosed by Li.

Response to Arguments

11. Applicant's arguments with respect to the pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. *Ahn et al. (Rapid Comm. Mass Spectr., 1999)* discloses "efficient analysis of oligosaccharide-malononitrile derivatives by on-line capillary liquid chromatography/electrospray ionization mass spectrometry" using a sheath liquid comprising acetonitrile and ammonium hydroxide for negative-mode ESI-MS; *Watkins et al. (Biochem. J., 1999)* discloses HPLC/MS/MS analysis of 8-epi-prostaglandin F_{2α} in a negative mode using the sheath gas flow. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yelena G. Gakh
8/9/04

